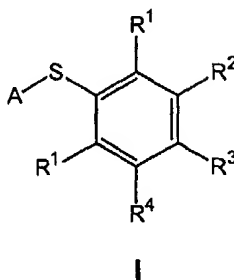## AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions and listings of claims in the application:
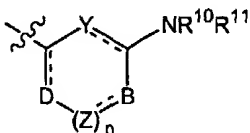
1. (currently amended) A compound of formula I

I

or a pharmaceutically acceptable salt or prodrug thereof,

wherein ~~at least one of R^1 or R^3 is a pyrimidine;~~

__R^1__, R^2, __R^3__, R^4 and R^5 are each independently selected from the group consisting

of hydrogen, halogen, alkyl, haloalkyl, alkoxy, cyano, nitro, cycloalkyl,

carboxaldehyde, ~~and~~ a group of formula II defined as

II

__and wherein at least one of R^1 or R^3 is a pyrimidine;__

subject to the proviso that one or more than one of R^1 or R^3 is a group of

formula II as defined above;

wherein ~~D~~, B, Y and Z ~~at each occurrence~~ are **each** independently selected from the group consisting of $-CR^6=$, $-CR^7R^8-$, $-C(O)-$, $-O-$, $-SO_2-$, $-S-$, $-N=$, and $-NR^9-$;

n is an integer of zero to three;

R^6, R^7, R^8 and R^9, ~~at each occurrence~~ are **each** independently selected from the group consisting of hydrogen, alkyl, carboxy, hydroxyalkyl, alkylaminocarbonylalkyl, dialkylaminocarbonylalkyl and carboxyalkyl; and

R^{10} and R^{11} are each independently selected from the group consisting of hydrogen, alkyl, cycloalkyl, alkoxyalkyl, alkoxycarbonylalkyl, carboxyalkyl, hydroxyalkyl, heterocyclyl, heterocyclylalkyl and heterocyclylamino; or

R^{10} and R^{11} are taken together with N to form a three to seven membered unsubstituted heterocyclyl ~~ring~~, or a three to seven membered substituted heterocyclyl ring, substituted with one or more than one substituent R^{13}, wherein R^{13}, ~~at each occurrence~~ is independently selected from the group consisting of alkyl, alkylene, alkoxy, alkoxyalkyl, cycloalkyl, aryl, heterocyclyl, heterocyclylalkyl, heterocyclylcarbonyl, heterocyclylalkylaminocarbonyl, hydroxy, hydroxyalkyl, hydroxyalkoxyalkyl, carboxy, carboxyalkyl, carboxycarbonyl, carboxaldehyde, alkoxycarbonyl, arylalkoxycarbonyl, aminoalkyl, aminoalkanoyl, aminocarbonyl, carboxamido, alkoxycarbonylalkyl, carboxamidoalkyl, cyano, tetrazolyl, alkanoyl, hydroxyalkanoyl, alkanoyloxy, alkanoylamino, alkanoyloxyalkyl, alkanoylaminoalkyl,

sulfonate, alkylsulfonyl, alkylsulfonylaminocarbonyl,

arylsulfonylaminocarbonyl and heterocyclylsulfonylaminocarbonyl;

wherein A is an unsubstituted aryl group, an unsubstituted heterocyclyl group, a

substituted aryl group, or a substituted heterocyclyl group, substituted with

one or more than one substituent R^{12}, wherein R^{12}, at each occurrence, is

independently selected from the group consisting of halogen, alkyl, aryl,

haloalkyl, hydroxy, alkoxy, alkoxyalkyl, alkoxycarbonyl, alkoxyalkoxy,

hydroxyalkyl, aminoalkyl, aminocarbonyl, alkyl(alkoxycarbonylalkyl)

aminoalkyl, heterocyclyl, heterocyclylalkyl, carboxaldehyde,

carboxaldehyde hydrazone, carboxamido, alkoxycarbonylalkyl, carboxy,

carboxyalkyl, carboxyalkoxy, hydroxyalkylaminocarbonyl, cyano, amino,

heterocyclylalkylamino, carboxythioalkoxy, carboxycycloalkoxy, thioalkoxy,

carboxyalkylamino, trans-cinnamyl and heterocyclylalkylaminocarbonyl;

and

wherein R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^8, R^9, R^{10}, R^{11}, R^{12} and R^{13} are unsubstituted

or substituted with one or more than one electron donating or electron
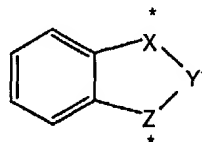
withdrawing group

wherein the heterocyclyl is chosen from **3-**, 4-, 5-, 6- and 7-membered rings

containing 1-3 heteroatoms independently selected from nitrogen, oxygen

and sulfur; the 4- and 5-membered rings have zero to two double bonds

and the 6- and 7-membered rings have zero to three double bonds, the

heterocycle **heterocyclyl** being optionally substituted with alkyl, halogen,

hydroxy or alkoxy substituents,

further wherein the heterocyclyl optionally comprises a group chosen from:

(i) bicyclic, tricyclic and tetracyclic groups in which any of the above heterocyclic rings is fused to one or two rings independently selected from an aryl ring, a cyclohexane ring, a cyclohexene ring, a cyclopentane ring, a cyclopentene ring, and another monocyclic heterocyclic ring;

(ii) bridged bicyclic groups where a monocyclic heterocyclic group is bridged by an alkylene group optionally selected from
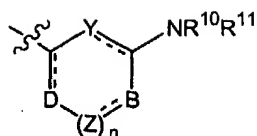

; and
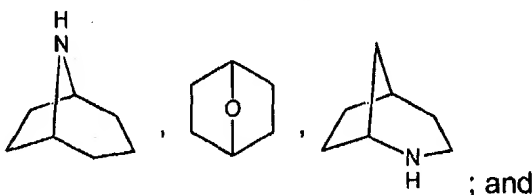
(iii) compounds of the formula where X* and Z* are **each** independently selected from -CH$_2$-, -CH$_2$NH-, -CH$_2$O-, -NH- and -O-, with the proviso that at least one of X* and Z* is not -CH$_2$-, and Y* is selected from -C(O)- and -(C(R")$_2$)$_v$ -, where R" is hydrogen or alkyl of one to four carbons, and v is 1-3.

2. (previously presented) A compound according to claim 1 wherein R^3 is the group of formula II
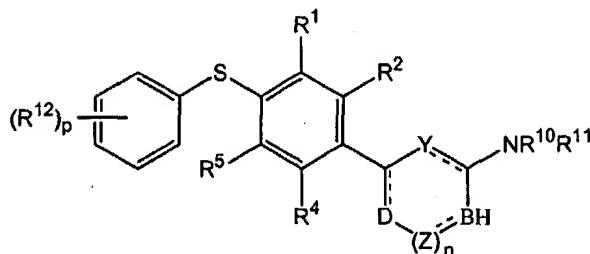
II

wherein R^{10}, R^{11}, D, B, Y, Z, and n are defined as in claim 1; and

R^1 is defined as in claim 1 with the proviso that if R^3 does not define a pyrimidine,

then R^1 is a pyrimidine.

3. (previously presented) A compound according to claim 1 of formula III

III

wherein R^1, R^2, R^4, R^5, R^{10}, R^{11}, R^{12}, D, B, Y, Z, and n are defined as in claim 1;

and p is an integer of zero to five.

4. (previously presented) A compound according to claim 3 wherein p is one;

R^4 and R^5 are hydrogen;

R^{12} is selected from the group consisting of halogen, alkyl, alkoxy,

carboxyalkoxy, carboxyalkyl and heterocyclyl;

R^{10} and R^{11} are taken together with N to form a three to seven membered

unsubstituted heterocyclyl ring, or a three to seven membered substituted

heterocyclyl ring, substituted with one or more than one subsituent R^{13},

wherein R^{13} is defined as in claim 1, and wherein said substituted

heterocyclyl, or unsubstituted heterocyclyl ring is selected from the group

consisting of piperidine, piperazine, morpholine, pyrrolidine, and azetidine;

and

wherein R^{10}, R^{11}, R^{12} and R^{13} are unsubstituted or substituted with at least one electron

donating or electron withdrawing group.

5. (previously presented) A compound according to claim 1 of formula IV
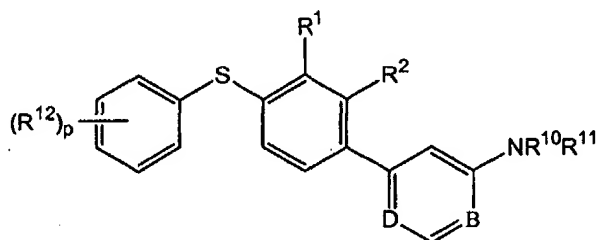
IV

wherein D and B are each independently selected from the group consisting of

   $-N=$ and $-CR^6=$;

R^1 is selected from the group consisting of hydrogen, halogen and haloalkyl, with

   the proviso that if R^3 does not define a pyrimidine, then R^1 is a pyrimidine;

R^2 is selected from the group consisting of hydrogen, halogen and haloalkyl;

R^{10} and R^{11} are defined as in claim 1;

R^{12}, at each occurrence, is independently selected from the group consisting of

   halogen, alkyl, haloalkyl, alkoxy, carboxyalkoxy, carboxyalkyl and

   heterocyclyl, wherein R^{12} is unsubstituted or substituted with at least one

   electron donating group or electron withdrawing group; and

p is an integer of zero to five.

6. (previously presented) A compound according to claim 5 wherein p is one; and

R^{10} and R^{11} are taken together with N to form a three to seven membered substituted heterocyclyl ring, or a three to seven membered unsubstituted heterocyclyl ring, substituted with one or more substituents R^{13}, wherein R^{13} is defined as in claim 1, and wherein said substituted heterocyclyl ring, or unsubstituted heterocyclyl ring is selected from the group consisting of piperidine, piperazine, morpholine, pyrrolidine, and azetidine.

7. (previously presented) A compound according to claim 1, selected from the group consisting of 1-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-piperidine-3-carboxylic acid, 4-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-6-(3-(2*H*-tetrazol-5-yl)-piperidin-1-yl)-pyrimidine, 4-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-6-(4-(2*H*-tetrazol-5-yl)-piperidin-1-yl)-pyrimidine, (1-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-piperidin-3-yl)-methanol, 2-(1-(6-(4-(2-isopropylphenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-piperidin-4-yl)-ethanol, 4-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-morpholine, 1-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-piperidin-4-ol, 4-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-2,5-dimethyl-morpholine, 1-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-piperidine-3-carboxylic acid amide, 1-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-piperidine-4-carboxylic acid amide, N-Ethyl-N-1-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-pyrrolidin-3-yl)-acetamide, 1-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-piperidine-3-carboxylic acid ethyl ester, 1-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-

phenyl)-pyrimidin-4-yl)-piperidine-4-carboxylic acid ethyl ester, 4-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-piperazine-1-carboxylic acid ethyl ester, 4-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-piperazin-1-yl-acetic acid ethyl ester, (3-imidazol-1-yl-propyl)-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-amine, 1-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-piperidine-4-carboxylic acid, 4-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-piperidine-3-carboxylic acid, 1-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-piperidine-3-carboxylic acid diethyl amide, N-1-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-pyrrolidin-3-yl)-acetamide, 4-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-6-(2-methoxymethyl-pyrrolidin-1-yl)-pyrimidine, 1-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-pyrrolidin-3-ol, (1-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-pyrrolidin-3-yl)-carbamic acid *tert*-butyl ester, isopropyl-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-methyl amine, and ethyl-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-methyl-amine.

8. (previously presented) A composition comprising:

    a compound according to claim 1

    and a pharmaceutically acceptable carrier.

9. (previously presented) A method of inhibiting inflammation or suppressing immune response in a mammal comprising administering to said mammal a therapeutic amount of a compound according to claim 1.

10. (previously presented) A compound according to claim 1 wherein A is

(i) an unsubstituted or substituted aryl group, substituted by one or more than one substituent R^{12}, wherein R^{12} is defined as in claim 1, or

(ii) an unsubstituted or substituted heterocyclyl group of the formula
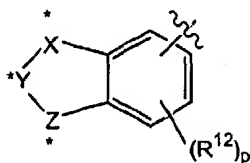
wherein

R^{12} and is defined as in claim 1;

p is an integer of 0 to 5;

X^* and Z^* are each independently selected from the group consisting of

$-CH_2-$, $-CH_2NH-$, $-CH_2O-$, $-NH-$, and $-O-$, with the proviso that at

least one of X^* and Z^* is not $-CH_2-$; and

Y^* is $-(C(R")_2)_v-$, wherein

R" is hydrogen or alkyl; and

v is 1, 2, or 3.

11. (previously presented) A compound according to claim 1 or 10 wherein A is an unsubstituted or substituted aryl group, wherein the aryl group is

(I) a mono- or a bicyclic carbocyclic ring system having one or two aromatic rings, or

(ii) a mono- or a bicyclic carbocyclic ring system having one or two aromatic rings,

wherein one or more than one of the aromatic rings is fused to a ring selected

from the group consisting of cyclohexane, cyclohexene, cyclopentane, and

cyclopentene.

12. (previously presented) A compound according to claim 1 wherein A is an

unsubstituted or substituted aryl group of the formula
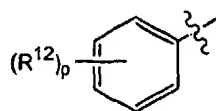
wherein R^{12} is defined as in claim 1; and p is an integer of 0 to 5.

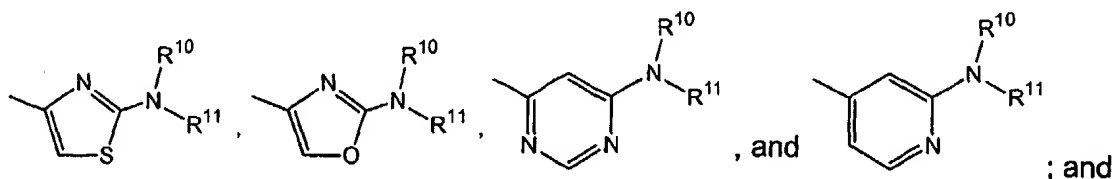13. (previously presented) A compound according to claim 1 wherein

D is $CR^6=$ or -N=,

B is -S-, -O-, -$CR^6=$ or -N=,

Y is -$CR^6=$ or -N=,

Z is -$CR^6=$ or -N=; and

n is zero or one.

14. (previously presented) A compound according to claim 1 wherein R^3 is selected

from the group consisting of

R^1 is defined as in claim 1 with the proviso that if R^3 does not define a pyrimidine,

then R^1 is a pyrimidine.

15. (previously presented) A compound according to claim 1 wherein,

D is -$CR^6=$;

B is -O- or -S-;

Y is -N=; and

n is zero.

16. (previously presented) A compound according to claim 1 wherein
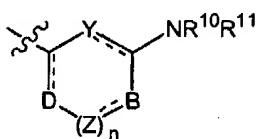
D is $-CR^6=$ or $-N=$;

B is $-N=$;

Y is $CR^6=$; and

n is 1.

17. (currently amended) A compound according to claim 1 wherein

R^1 is selected from the group consisting of hydrogen, halogen, alkyl, and nitro,

and   **wherein R^{10}, R^{11}, D, B, Y, Z, and n are defined**

as in claim 1, with the proviso that if R^3 does not define a pyrimidine, then

R^1 is a pyrimidine;

R^2 is selected from the group consisting of hydrogen, halogen, alkyl, and nitro;

R^4 and R^5 are each independently selected from the group consisting of

hydrogen and alkyl; and

R^3 is
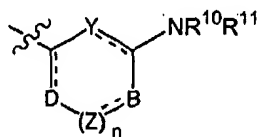
wherein

D is $-CR^6=$ or $-N=$,

B is -S-, -O-, -CR^6= or -N=,

Y is -CR^6= or -N=,

Z is -CR^6= or -N=; and

n is zero or one

18. (previously presented) A compound according to claim 1 wherein

R^1 and R^2 are each independently selected from the group consisting of

hydrogen, halogen, and haloalkyl;

R^3 is a pyrimidine; and

R^4 and R^5 are each independently hydrogen.

19. (currently amended) A compound according to claim 1 wherein

R^1 is selected from the group consisting of hydrogen, halogen, and haloalkyl,
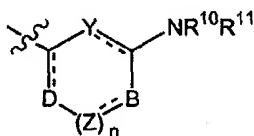

and _____ wherein R^{10}, R^{11}, D, B, Y, Z, and n are defined

as in claim 1, with the proviso that if R^3 does not define a pyrimidine, then

R^1 is a pyrimidine;

R^2 is selected from the group consisting of hydrogen, halogen, and haloalkyl;

R^4 and R^5 are each independently hydrogen; and

R^3 is

wherein

D is -CR^6= or -N=,

B is -S-, -O-, -CR^6= or -N=,

Y is -CR^6= or -N=,

Z is -CR^6= or -N=; and

n is zero or one.

20. (currently amended) A compound according to claim 1 wherein

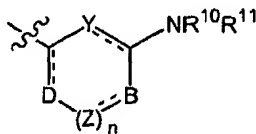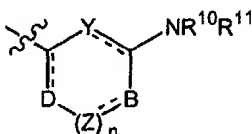R^1 is selected from the group consisting of hydrogen, halogen, and haloalkyl,

and wherein R^{10}, R^{11}, D, B, Y, Z, and n are d fin d

as in claim 1, with the proviso that if R^3 does not define a pyrimidine, then

R^1 is a pyrimidine;

R^2 is selected from the group consisting of hydrogen, chloro, and trifluoromethyl;

R^4 and R^5 are each independently hydrogen; and

R^3 is selected from the group consisting of
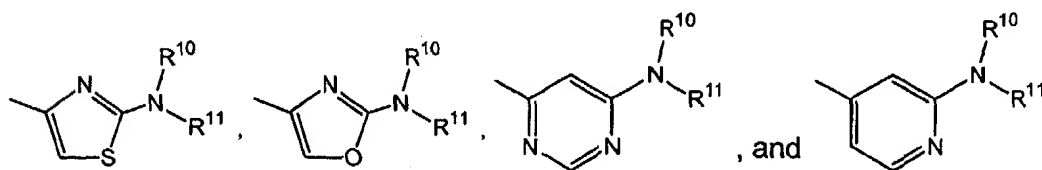
21. (previously presented) A compound according to claim 1 wherein R^6 is hydrogen.

22. (previously presented) A compound according to claim 1 wherein

R^1 is selected from the group consisting of hydrogen, halogen and haloalkyl,

R^2 is selected from the group consisting of hydrogen and halogen,

R^3 is a pyrimidine, and

R^4 and R^5 are each hydrogen.

23. (previously presented) A compound according to claim 22 wherein

R^1 is trifluoromethyl,

R^2 is hydrogen, and

R^3 is a pyrimidine.

24. (previously presented) A compound according to claim 22 wherein R^1 and R^2 are each chloro, and R^3 is a pyrimidine.

25. (previously presented) A compound according to claim 1 which has an IC_{50} of less than 20 μM when tested in one or both of

(i) an ICAM-1/LFA-1 Biochemical Interaction Assay, or

(ii) an ICAM-1/JY-8 Cell Adhesion Assay

26. (previously presented) A method for ameliorating a pathology in a mammal arising from the interaction of LFA-1 with ICAM-1 or ICAM-3 comprising administering to said mammal a therapeutic amount of a compound according to claim 1.

27. (previously presented) A method according to claim 26 wherein the pathology is selected from an inflammatory disease, an autoimmune disease, tumor metastasis, allograft rejection and reperfusion injury.

REMARKS

I.   Status of the Claims

Claims 1-27 are pending in the application. Claims 1, 17, 19, and 20 have been amended. Claim 15 is withdrawn from consideration.

Claim 1 has been amended to require that R^1 and R^3 be selected from the recited group. In light of this amendment to claim 1, dependent claims 17, 19, and 20 have

been amended to expand the recited group for R^1 to include the compound of formula II. These amendments are also consistent with the existing provisos in claims 17, 19, and 20 that R^1 be a pyrimidine if R^3 does not define a pyrimidine.

Claim 1 has also been amended to define heterocyclyl as chosen from **3-**, 4-, 5-, 6- and 7-membered rings to render this definition consistent with the definition of unsubstituted and substituted heterocyclyl for R^{10} and R^{11}. Other minor amendments have been made for the purposes of clarity.

No new matter has been added by these amendments, nor do these amendments raise new issues or necessitate the undertaking of any additional search of the art by the Examiner. Accordingly, Applicants respectfully request further examination of the claims.

The Examiner recommends that claim 15 be deleted, asserting that it is drawn to a non-elected invention. *Final Office Action* at p. 2. Applicants respectfully disagree. Dependent claim 15 can define a non-pyrimidine so long as the compound of formula I includes a pyrimidine at the R^1 or R^3 position, a proviso that is explicitly recited in independent claim 1. Accordingly, Applicants respectfully request examination of claim 15.

II.   Objection to the claims

The Examiner has objected to claim 13 as allegedly "drawn to multiple inventions for reasons set forth in the restriction requirement." *Final Office Action* at p. 2. The Examiner further states that "only one of R^1 or R^3 is permitted to be a pyrimidine ring." *Id.* at 3.

Applicants respectfully disagree. Both R^1 or R^3 can be a pyrimidine so long as at least one of R^1 or R^3 defines a group of formula II, which can be a pyrimidine. Stated otherwise, R^1 and/or R^3 can be both a group of formula II and a pyrimidine. Claim 13 further limits the group of formula II such that D, B, Y, and Z are chosen from specified radicals. Claim 13 can read on the elected invention whether or not the group of formula II defines a pyrimidine. For example, if claim 13 defines a group of formula II that is not a pyrimidine and this group is assigned as R^3, then R^1 is necessarily a pyrimidine (and vice versa). Thus, claim 13 does not have to define a pyrimidine to read on the elected invention by virtue of the proviso in claim 1 requiring that at least one of R^1 or R^3 be a pyrimidine.

Finally, Applicants respectfully disagree that "only one of R^1 or R^3 is a pyrimidine as was done in claim 20." *Id.* In claim 20, the R^3 is selected from four substituents. The third substituent is a pyrimidine. Thus, if R^3 is not a pyrimidine, the proviso of claim 20 requires that R1 be a pyrimidine. If R^3 is a pyrimidine, the proviso does not exclude R^1 from being a pyrimidine. Moreover, claim 20 has been amended to clarify this existing proviso to allow R^1 to be selected from the group of formula II, which can define a pyrimidine.

Accordingly, it is respectfully requested that the objection to claim 13 be withdrawn.

III.   **Rejection under 35 U.S.C. § 112, second paragraph**

Claims 1-14 and 16-27 are rejected under 35 U.S.C. § 112, second paragraph as being indefinite. *Final Office Action* at pp. 3-4. Applicants respectfully traverse this rejection.

The Examiner believes that the proviso "one or more than one of R^1 or R^3 is a group of formula II as defined above" is not clear. *Id.* at p. 3. The Examiner questions how "more than one of R^1 or R^3 is a group of formula II, when applicants indicate that at least one of R^1 or R^3 is a pyrimidine." *Id.*

Definiteness under 35 U.S.C. § 112, second paragraph is determined from the point of view of one of ordinary skill in the art. M.P.E.P. § 2173.02. ("[T]he examiner must consider the claim as a whole to determine whether the claim apprises one of ordinary skill in the art of its scope."). Applicants respectfully submit that one of ordinary skill in the art would appreciate that radicals encompassed by formula II are not mutually exclusive from pyrimidines. As stated above, R^1 and/or R^3 can be both a group of formula II and a pyrimidine. Applicants provide some examples of compounds that fall within the elected invention:

> Example 1. R^1 is a pyrimidine of any formula and R^3 is a non-pyrimidine of formula II. (*see, e.g.*, proviso of claim 2). Here, only one of R^1 and R^3 is a pyrimidine and only one of R^1 and R^3 is a group of formula II.
>
> Example 2. R^1 is a pyrimidine but not of formula II and R^3 is a pyrimidine of formula II. Here, both of R^1 and R^3 are pyrimidines and only one of R^1 and R^3 is a group of formula II.
>
> Example 3. R^1 is a pyrimidine of formula II and R^3 is a pyrimidine of formula II. Here, both of R^1 and R^3 are pyrimidines and both of R^1 and R^3 are groups of formula II.

The claimed invention does not cover the scenarios where neither R^1 and R^3 is a pyrimidine or neither R^1 and R^3 is a group of formula II.

Applicants respectfully submit that the claim as presented in the previous response to the office action is sufficiently clear. Nevertheless, claim 1 has been amended in accordance with the Examiner's second suggested amendment at p. 4. Claim 1, as amended, defines R^1 and R^3 as being chosen from the same list of substituents as for R^2, R^4, and R^5. The provisos remain unamended.

Accordingly, Applicants respectfully request withdrawal of this rejection.

IV. Conclusion

In view of the foregoing amendments and remarks, Applicants respectfully request the reconsideration and reexamination of this application and the timely allowance of the pending claims. If the Examiner believes a telephone conference would be useful in resolving any outstanding issues, he is invited to call the undersigned at (617) 452-1621.

Please grant any extensions of time required to enter this response and charge any additional required fees to our Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P

By: _Maria Bautista_
Maria T. Bautista
Reg. No. 52,516

Date: November 5, 2003